Applicant: T. Keith Blackwell et al. Attorney's Docket No.: 10276-0093US1

Serial No.: 10/560,563

Filed: February 15, 2007

Page : 2 of 11

## Amendments to the Specification

Please replace the paragraph beginning at page 15, line 31, with the following amended paragraph:

Figs. 3A-3C: Specific elements required for skn-1-independent and -dependent GCS-1::GFP expression. 3A: Analysis of the gcs-1 promoter. Expression of the indicated constructs from transgenic extrachromosomal arrays was assayed in 2-3 independent transgenic lines, under normal conditions and after induction by paraquat and heat. Approximate relative expression levels in the tissues designated to the right (data not shown) are indicated by + signs, with ++ indicating a reproducible reduction, and + indicating barely detectable expression. Within each set of transgenic lines that carried promoter mutations, levels of normal and induced expression were affected in parallel. Mutations that were created in predicted SKN-1 sites 1, 2, and 3 are described in Materials and Methods, and are not compatible with SKN-1 binding (see text). [[Red]] Grey ovals indicate predicted SKN-1 binding sites and a grey green bar the 5' end of the gcs-1::gfp coding region. Map numbers refer to the predicted translation start. 3B: Uncoupling pharyngeal GCS-1::GFP expression from intestinal and ASI neuron expression. The gcs∆ 2 mutation eliminated pharyngeal GCS-1::GFP expression, but allowed near-wild type levels of ASI and intestinal expression. Concurrent ablation of SKN-1 binding site 3 (gcs\Delta) 2,mut3) eliminated transgene expression in all tissues. Paraquat-treated worms are shown in the GFP column. 3C: Composite gcs-1 promoter element that includes SKN-1 site 3, and is also present in the med-1 and -2 promoters. SKN-1 binding sites are in a lighter grey font[[red]], and identical sequences are boxed.

Please replace the paragraph beginning at page 16, line 31, with the following amended paragraph:

Figs. 5A-5G: Expression and stress-induced nuclear accumulation of SKN-1::GFP. 5A: SKN-1::GFP transgenes **a.** *skn-1* gene. Transcribed coding and untranslated regions are indicated in red and blue dark grey and light grey, respectively. **b.** SKN-1::GFP translational

Applicant: T. Keith Blackwell et al. Attorney's Docket No.: 10276-0093US1

Serial No.: 10/560,563

Filed: February 15, 2007

Page : 3 of 11

fusion construct, which includes an EcoR1 fragment that previously rescued maternal skn-1 lethality. C. elegans DNA is indicated by a black line. c. SknPro::GFP promoter fusion, in which the 38 N-terminal SKN-1 amino acids are fused to GFP containing a nuclear localization signal. 5B-5D: Embryonic expression of SKN-1::GFP. 5B, 5C, and 5D show Nomarski (left) and fluorescent (right) views, of 100 cells, 280 min., and three fold embryos, respectively. Endogenous intestinal autofluorescence [[is]] was visible as yellow or orange in the original. White triangles indicate intestine precursor nuclei. Int: intestine. Ph: pharynx. 5E: SKN-1::GFP expression in ASI neurons (arrows). Nomarski/fluorescent (left) and fluorescent (right) views are shown of a typical DiI-exposed L4 larva. 5F: Larval SKN-1::GFP expression under normal conditions. Fluorescent and Nomarski closeups of the boxed region of this L2 are shown at bottom. Note the low-level SKN-1::GFP expression in intestinal nuclei (white triangle). 5G: SKN-1::GFP localization under oxidative stress. Examination of multiple focal planes revealed that SKN-1::GFP levels were not substantially altered in ASI neurons (arrows), but in many animals were dramatically increased in intestinal nuclei (Table 3). A heat-shocked L2 is shown. but similar results were obtained upon exposure to other oxidative stress inducers (Table 3). The integrated strain Is007 is shown, but two extrachromosomal lines and a different integrated line exhibited similar patterns.